

PATENT COOPERATION TREATY
PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rule 843 and 44)

Applicant's or agent's file reference 365.100	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/US 99/09346	International filing date (day/month/year) 30/04/1999	(Earliest) Priority Date (day/month/year) 01/05/1998
Applicant CHIRON CORPORATION et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of **11** sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished
- 2. Certain claims were found unsearchable (See Box I).
- 3. Unity of invention is lacking (see Box II).
- 4. With regard to the title,
 - the text is approved as submitted by the applicant.
 - the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

1a

None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1. Claims: 1,3,16,18 (all completely); 2,4-15,17 (all partially)

A protein comprising the amino sequence of SEQ ID NO:2790 or comprising a fragment of at least 7 (preferably consecutive) amino acids of said SEQ ID NO; a protein with 50% or greater homology to said protein(s); an antibody binding to said protein(s); a nucleic acid encoding said protein(s), preferably comprising the nucleotide sequence of SEQ ID NO:2789 or a fragment comprising 10 or more consecutive nucleotides thereof; complementary nucleic acid molecules; compositions comprising said protein(s), nucleic acid(s) or antibody for vaccination, diagnosis or pharmaceutical use, preferably immunogenic compositions comprising said protein(s), and the use of said composition(s).

Invention 2. Claims: 2,4-15,17 (all partially)

A protein comprising an amino sequence according to SEQ ID NO:2 or comprising a fragment of at least 7 consecutive amino acids of said SEQ ID NO; an antibody binding to said protein(s); a nucleic acid encoding said protein(s), preferably comprising a nucleotide sequence according to SEQ ID NO:1 or a fragment comprising 10 or more consecutive nucleotides thereof; complementary nucleic acid molecules; compositions comprising said protein(s), nucleic acid(s) or antibody for vaccination, diagnosis or pharmaceutical use, preferably immunogenic compositions comprising said protein(s), and the use of said composition(s).

Inventions 3-1510. Claims: 2,4,-15,17 (all partially)

Same as invention 2 but for proteins limited to the even-numbered SEQ ID NOs:4-3020 except 2790, and for nucleic acids limited to the corresponding odd-numbered SEQ ID NOs:3-3019 except 2789. E.g., invention 3: limited to SEQ ID NO:4 and SEQ ID NO:3, invention 4: limited to SEQ ID NO:6 and SEQ ID NO:5, . . . , invention 1509: limited to SEQ ID NO:3018 and SEQ ID NO:3017, and invention 1510: limited to SEQ ID NO:3020 and SEQ ID NO:3019.

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1,3,16,18 (all completely); 2,4-15,17 (all partially). Inventions searched:
#1 (SEQ ID NOS 2789/2790), #2 (1/2), #222 (441/442), #246 (489/490), #602 (1201/1202), #729 (1455/1456), #874 (1745/1746), #1397 (2791/2792)

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/31 C07K 22 C07K16/12 C12Q1/68 A61K39/095
G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K C12Q A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE TREMBL [Online] EMBL ID Q55666, AC Q55666, 1 November 1996 (1996-11-01) TABATA S: "Membrane-bound lytic transglycosylase A MltA Synechocystis sp. strain PCC 6803" XP002130156 Note: 100% aa seq identity of aa 342-350 with aa 392-400 of SEQ ID NOS 2790 and 2792, 27.6% (26.9%) aa seq identity with SEQ ID NO:2790 (2792) in 370 (387) aa overlap. the whole document</p> <p>---</p> <p>-/-</p>	1,4-6,9, 12

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

26 May 2000

Date of mailing of the international search report

15.06.00

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 818 465 A (BIOLOG MOLECULAIRE DES PLANTES ; INST OF MOLECULAR BIOTECHNOLOGY (DE) 14 January 1998 (1998-01-14) Note: 100% nt seq identity of nt 367951-367961 of SEQ ID NO:1 with nt 163-173 of SEQ ID NO:2789. page 108 ---	8,11,12
A	LOMMATZSCH J ET AL.: "Outer membrane localization of murein hydrolases: MltA, a third lipoprotein lytic transglycosylase in Escherichia coli" JOURNAL OF BACTERIOLOGY, vol. 179, no. 17, September 1997 (1997-09), pages 5465-5470, XP002130154 Note: 33.7% (35.7%) aa seq identity with SEQ ID NO:2790 (2792) in 273 (207) aa overlap. abstract ---	1-12
A	DILLARD J P ET AL.: "A peptidoglycan hydrolase similar to bacteriophage endolysins acts as an autolysin in Neisseria gonorrhoeae" MOLECULAR MICROBIOLOGY, vol. 25, no. 5, September 1997 (1997-09), pages 893-901, XP000878964 abstract ---	1-12
A	WO 96 29412 A (IAF BIO VAC INC ; BRODEUR BERNARD R (CA); MARTIN DENIS (CA); HAMEL) 26 September 1996 (1996-09-26) cited in the application the whole document examples 1-12 ---	1-18
A	WO 94 08013 A (OREGON STATE) 14 April 1994 (1994-04-14) the whole document examples 1-7 ---	1-18
A	WO 92 13871 A (UNIV WASHINGTON) 20 August 1992 (1992-08-20) the whole document examples 1-10 ---	1-18
A	BLAKE M S ET AL.: "Vaccines for gonorrhoea: where are we on the curve?" TRENDS IN MICROBIOLOGY, vol. 3, no. 12, December 1995 (1995-12), pages 469-474, XP000876514 the whole document ---	1-18
	-/-	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
A	POOLMAN J T: "Development of a meningococcal vaccine" INFECTIOUS AGENTS AND DISEASE, vol. 4, no. 1, March 1995 (1995-03), pages 13-28, XP000876540 the whole document ---	1-18
X	WO 96 01901 A (RHONE POULENC RORER SA ;BLANC VERONIQUE (FR); THIBAUT DENIS (FR);) 25 January 1996 (1996-01-25) Note: 100% nt seq ident of bp 170-156 of SEQ ID NO:1 (rev DNA) with bp 202-216 of SEQ ID NO:1 (61.2% in 348 bp overlap), 40.7% seq ident of transl SEQ ID NO:1 with SEQ ID NO:2 in 118 aa overlap. page 102-104 example 1 ---	8,11,12
X	WO 97 37044 A (ASTRA AB ;ALM RICHARD A (US); SMITH DOUGLAS (US)) 9 October 1997 (1997-10-09) Note: 100% aa seq identity of aa 204-211, 186-193 & 352-359 of transl SEQ ID NOs 227, 345 & 1003, resp., with aa 59-66 of SEQ ID NO:2, 37.4% aa seq identity with SEQ ID NO:2 in 115 aa overlap. page 268-269 page 344 page 909-910 page 23, paragraph B.4 ---	4,12-14
X	DATABASE SWISSPROT [Online] ID YPCP_YEREN, AC P31485, 1 July 1993 (1993-07-01) BAEUMLER A J ET AL.: "Hypothetical 29.6 kD protein in PCP 5' region (ORF1)" XP002138650 Note: 100% aa seq identity of aa 148-159 with aa 140-151 of SEQ ID NO:442, 43.4% aa seq identity with SEQ ID NO:442 in 256 aa overlap. the whole document -& BAUMLER A J ET AL.: "A lipoprotein of Yersinia enterocolitica facilitates ferrioxamine uptake in Escherichia coli" JOURNAL OF BACTERIOLOGY, vol. 174, no. 3, February 1992 (1992-02), pages 1029-1035, XP000907295 page 1031, left-hand column, line 11 -right-hand column, line 15 ---	4,12
A	-/-	4,12

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Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE SWISSPROT [Online] ID YDHH_HAEIN, AC P44861, 1 November 1995 (1995-11-01) FLEISCHMANN R D ET AL.: "Hypothetical protein HI0753" XP002138651 Note: 100% aa seq identity of aa 143-156 with aa 140-153 of SEQ ID NO:442, 41.6% aa seq identity with SEQ ID NO:442 in 377 aa overlap. the whole document</p> <p>---</p>	4,12
X	<p>WO 96 33276 A (HUMAN GENOME SCIENCES INC ;UNIV JOHNS HOPKINS (US)) 24 October 1996 (1996-10-24)</p> <p>Note: 100% nt seq identity of bp 816794-816807 with bp 289-302 of SEQ ID NO:441 (54.3% in 484 bp overlap), 100% aa seq identity of translated sequence with SEQ ID NO:442 in 14 aa overlap.</p> <p>page 77.488</p> <p>Note: 100% nt seq identity of bp 230516-230526 with bp 1501-1511 of SEQ ID NO:489 (57.4% in 1292 bp overlap), 100% aa seq identity of translated sequence with SEQ ID NO:490 in 13 aa overlap.</p> <p>page 77.139</p> <p>page 76.37, line HI0215</p> <p>Note: 100% nt seq identity of bp 1025409-1025418 with bp 1339-1330 (rev strand) of SEQ ID NO:1201 (72.0% in 50 bp overlap).</p> <p>page 77.612</p> <p>---</p>	4,8, 11-14
X	<p>CONLIN C A ET AL.: "Escherichia coli prlC encodes an endopeptidase and is homologous to the Salmonella typhimurium opdA gene" JOURNAL OF BACTERIOLOGY, vol. 174, no. 18, September 1992 (1992-09), pages 5881-5997, XP000907300</p> <p>Note: 100% nt seq ident of bp 1824-1837 with bp 1480-1493 of SEQ ID NO:489 (59.7% in 1282 bp overlap), 100% aa seq ident of aa 495-507 with aa 492-504 of SEQ ID NO:490 (49.5% in 679 aa overlap).</p> <p>abstract</p> <p>figure 2</p> <p>---</p> <p>-/-</p>	4,8,11, 12

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Category °	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE SWISSPROT [Online] ID OPDA_HAEIN, AC P44573, 1 November 1995 (1995-11-01) FLEISCHMANN R D ET AL.: "Oligopeptidase A (EC 3.4.24.70)" XP002138652 Note: 100% aa seq identity of aa 496-508 with aa 492-504 of SEQ ID NO:490, 49.0% aa seq identity in 677 aa overlap. the whole document</p> <p>---</p>	4,12
X	<p>ROKBI B ET AL.: "Evaluation of recombinant transferrin - binding protein B variants from <i>Neisseria meningitidis</i> for their ability to induce cross-reactive and bactericidal antibodies against a genetically diverse collection of serogroup B strains." <i>INFECTION AND IMMUNITY</i>, vol. 65, no. 1, January 1997 (1997-01), pages 55-63, XP002138643 abstract</p> <p>---</p>	5
P,A	<p>DATABASE TREMBL [Online] EMBL ID 069750, AC 069750, 1 August 1998 (1998-08-01) ROKBI B ET AL.: "Transferrin binding protein B, TbpB, <i>Neisseria meningitidis</i>" XP002138653 Note: 22.3% aa seq identity with SEQ ID NO:1202 in 488 aa overlap. the whole document</p> <p>-& ROKBI B ET AL.: "Heterogeneity of tpbB, the transferrin-binding protein B gene, among serogroup B <i>Neisseria meningitidis</i> strains of the ET-5 complex" <i>CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY</i>, vol. 4, no. 5, September 1997 (1997-09), pages 522-529, XP002138644 abstract</p> <p>---</p>	4,8, 12-15,17
A	<p>---</p> <p>-/-</p>	5,8, 12-15,17

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Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE GCG_GENESEQ [Online] ID W14640, AC_W14640, 5 March 1998 (1998-03-05) QUENTIN-MILLET M J ET AL.: "N. meningitidis HTR Tbp2 (del3777-385, del1407-465, del1488-508)" XP002138654 Note: 23.5% aa seq identity with SEQ ID NO:1202 in 571 aa overlap. the whole document -& WO 97 13860 A (PASTEUR MERIEUX SERUMS VACC; QUENTIN MILLET MARIE JOSE (FR); ROKBI)) 17 April 1997 (1997-04-17) claim 11 ---	4,8, 12-15,17
A	DATABASE EMPR01 [Online] EMBL ID AF034831, AC AF034831, 4 December 1997 (1997-12-04) YOU Z ET AL.: "Rhizobium etli stomatin like protein (slp) gene, complete cds." XP002138655 Note: 100% nt seq ident of bp 4384-4395 with bp 529-540 of SEQ ID NO:1455 (54.4% in 638 bp overlap), 100% aa seq ident of aa 1394-1403 with aa 109-118 of SEQ ID NO:1456 (41.2% in 182 aa overlap). the whole document -& YOU Z ET AL.: "A stomatin-like protein encoded by the slp gene of Rhizobium etli is required for nodulation competitiveness on the common bean" MICROBIOLOGY, vol. 144, no. 9, September 1998 (1998-09), pages 2619-2627, XP000907294 abstract figure 2 ---	4,8,11, 12
P,X	HUANG M ET AL.: "A stomatin-like protein necessary for mechanosensation in C. elegans" NATURE, vol. 378, no. 6554, 16 November 1995 (1995-11-16), pages 292-295, XP002138646 Note: 100% aa seq identity of aa 233-239 with aa 110-117 of SEQ ID NO:1456, 29.9% aa seq identity in 234 aa overlap. abstract figure 1 ---	4,8,11, 12
X		4,12
		-/-

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WONG C Y ET AL.: "Cloning and characterization of two immunophilin-like genes, ilpA and fkpA, on a single 3.9-kilobase fragment of <i>Aeromonas hydrophila</i> genomic DNA" <i>JOURNAL OF BACTERIOLOGY</i>, vol. 179, no. 11, June 1997 (1997-06), pages 3397-3403, XP002138647 Note: 100% nt seq ident of bp 2659-2672 with bp 613-626 of SEQ ID NO:1745 (59.2% in 655 bp overlap), 100% aa seq ident of aa 205-216 with aa 200-211 of SEQ ID NO:1746 (44.9% in 265 aa overlap).</p> <p>abstract figure 2</p> <p>---</p>	4,8, 11-14
X	<p>DATABASE EMPR02 [Online] EMBL ID NE01198, AC U001198, 23 November 1993 (1993-11-23)</p> <p>MCALLISTER C F ET AL.: "Neisseria elongata NRL FKBP immunophilin homolog gene" XP002138656 Note: 100% nt seq identity of bp 125-138 with bp 635-648 of SEQ ID NO:1745 (65.8% nt seq identity in 237 bp overlap).</p> <p>the whole document</p>	8,11,12
X	<p>-& MCALLISTER C F ET AL.: "Analysis in <i>Neisseria meningitidis</i> and other <i>Neisseria</i> species homologous to the FKBP immunophilin family" <i>MOLECULAR MICROBIOLOGY</i>, vol. 10, no. 1, October 1993 (1993-10), pages 13-23, XP000907304 abstract figure 3</p> <p>---</p>	8,11,12
X	<p>SAMPSON B A ET AL.: "Neisseria meningitidis encodes an FK506-inhibitable rotamase" PROC. NAT'L. ACAD. SCI. USA, vol. 89, no. 4, 15 February 1992 (1992-02-15), pages 1164-1168, XP002138648 Note: 100% nt seq identity of bp 278-288 (284-294) with bp 719-729 of SEQ ID NO:1745 (60.5% nt seq identity in 281 bp overlap).</p> <p>abstract figure 2</p> <p>---</p> <p>-/-</p>	8,11,12

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
A	HACKER J ET AL.: "Immunophilins: structure-function relationship and possible role in microbial pathogenicity." MOLECULAR MICROBIOLOGY, vol. 10, no. 3, November 1993 (1993-11), pages 445-456, XP000907321 abstract ---	13,14,17
X	DATABASE EMPR01 [Online] EMBL ID ECUW93, AC U14003 (partial), 30 November 1994 (1994-11-30) BURLAND V ET AL.: "Escherichia coli K-12 chromosomal region from 92.8 to 00.1 minutes" XP002138657 Note: 100% nt seq identity of bp 37827-37839 with bp 1186-1174 of SEQ ID NO:2791. page 4 -----	8,11,12

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Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0818465	A 14-01-1998	EP 0917582 A WO 9802560 A		26-05-1999 22-01-1998
WO 9629412	A 26-09-1996	AU 716225 B AU 4934396 A BR 9607651 A CA 2215161 A CZ 9702914 A EP 0815234 A HU 9702387 A JP 11500624 T NO 974264 A PL 322363 A SI 9620035 A SK 125597 A		24-02-2000 08-10-1996 17-11-1998 26-09-1996 14-01-1998 07-01-1998 28-05-1998 19-01-1999 13-11-1997 19-01-1998 31-12-1998 03-06-1998
WO 9408013	A 14-04-1994	AU 5403594 A		26-04-1994
WO 9213871	A 20-08-1992	AU 1411492 A US 5834591 A		07-09-1992 10-11-1998
WO 9601901	A 25-01-1996	FR 2722210 A AP 562 A AU 712397 B AU 2891295 A BR 9508714 A CA 2193130 A CN 1152338 A CZ 9700052 A EP 0770132 A HU 77341 A JP 10502532 T NO 970047 A NZ 289153 A PL 318193 A SK 597 A TR 960040 A ZA 9505688 A		12-01-1996 20-11-1996 04-11-1999 09-02-1996 02-06-1998 25-01-1996 18-06-1997 14-05-1997 02-05-1997 30-03-1998 10-03-1998 07-01-1997 25-02-1999 26-05-1997 06-08-1997 21-06-1996 26-02-1996
WO 9737044	A 09-10-1997	AU 2598497 A BR 9708456 A CA 2248985 A CN 1220703 A CZ 9802976 A EP 0901530 A JP 2000501621 T NO 984517 A PL 329045 A SK 130598 A		22-10-1997 03-08-1999 09-10-1997 23-06-1999 17-02-1999 17-03-1999 15-02-2000 25-11-1998 01-03-1999 11-06-1999
WO 9633276	A 24-10-1996	AU 5552396 A CA 2218741 A EP 0821737 A JP 11501520 T		07-11-1996 24-10-1996 04-02-1998 09-02-1999
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9713860 A		EP 0796332 A HU 9801714 A JP 11500630 T NO 972314 A	24-09-1997 28-10-1998 19-01-1999 18-07-1997